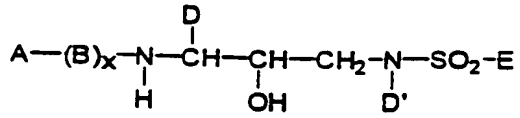
CLAIMS

We claim:

1. A compound of formula I:



(I)

wherein:

A is selected from the group consisting of H; Het; $-R^1$-Het; $-R^1-C_1-C_6$ alkyl, which may be optionally substituted with one or more groups selected from the group consisting of hydroxy, C_1-C_4 alkoxy, Het, -O-Het, $-NR^2-CO-N(R^2)(R^2)$ and $-CO-N(R^2)(R^2)$; and $-R^1-C_2-C_6$ alkenyl, which may be optionally substituted with one or more groups selected from the group consisting of hydroxy, C_1-C_4 alkoxy, Het, -O-Het, $-NR^2-CO-N(R^2)(R^2)$ and $-CO-N(R^2)(R^2)$;

each R^1 is independently selected from the group consisting of $-C(O)-$, $-S(O)_2-$, $-C(O)-C(O)-$, $-O-C(O)-$, $-O-S(O)_2$, $-NR^2-S(O)_2-$, $-NR^2-C(O)-$ and $-NR^2-C(O)-C(O)-$;

each Het is independently selected from the group consisting of C_3-C_7 cycloalkyl; C_5-C_7 cycloalkenyl; C_6-C_{10} aryl; and 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, $N(R^2)$, O, S and $S(O)_n$, wherein said heterocycle may optionally be benzofused; and wherein any member of said Het may be optionally substituted with one or more substituents selected from the group consisting of oxo, $-OR^2$, $-R^2$, $-N(R^2)(R^2)$, $-R^2-OH$, -CN, $-CO_2R^2$, $-C(O)-N(R^2)(R^2)$, $-S(O)_2-N(R^2)(R^2)$, $-N(R^2)-C(O)-R^2$, $-C(O)-R^2$, $-S(O)_n-R^2$, $-OCF_3$, $-S(O)_n-Ar$, methylenedioxy, $-N(R^2)-S(O)_2(R^2)$, halo, $-CF_3$, $-NO_2$, Ar and -O-Ar;

each R^2 is independently selected from the group consisting of H and C_1-C_3 alkyl optionally substituted with Ar;

B, when present, is $-N(R^2)-C(R^3)(R^3)-C(O)-$;

x is 0 or 1;

each R^3 is independently selected from the group consisting of H, Het, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_6 cycloalkyl and C_5-C_6 cycloalkenyl, wherein any member of said R^3, except H, may be optionally substituted with one or more substituents selected from the group consisting of $-OR^2$, $-C(O)-NH-R^2$, $-S(O)_n-N(R^2)(R^2)$, Het, $-CN$, $-SR^2$, $-CO_2R^2$, $NR^2-C(O)-R^2$;

each n is independently 1 or 2;

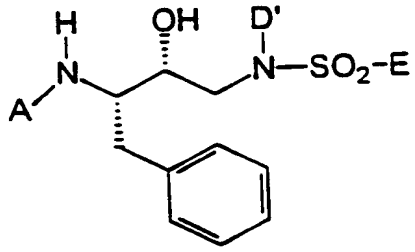
D and D' are independently selected from the group consisting of Ar; C_1-C_4 alkyl, which may be optionally substituted with one or more groups selected from C_3-C_6 cycloalkyl, $-OR^2$, $-R^3$, -O-Ar and Ar; C_2-C_4 alkenyl, which may be optionally substituted with one or more groups selected from the group consisting of C_3-C_6 cycloalkyl, $-OR^2$, $-R^3$, -O-Ar and Ar; C_3-C_6 cycloalkyl, which may be optionally substituted with or fused with Ar; and C_5-C_6 cycloalkenyl, which may be optionally substituted with or fused with Ar;

each Ar is independently selected from the group consisting of phenyl; 3-6 membered carbocyclic ring and 5-6 membered heterocyclic ring containing one or more heteroatoms selected from O, N, S, $S(O)_n$ and $N(R^2)$, wherein said carbocyclic or heterocyclic ring may be saturated or unsaturated and optionally substituted with one or more groups selected from the group consisting of oxo, $-OR^2$, $-R^2$, $-N(R^2)(R^2)$, $-N(R^2)-C(O)-R^2$, $-R^2-OH$, $-CN$, $-CO_2R^2$, $-C(O)-N(R^2)(R^2)$, halo and $-CF_3$;

E is selected from the group consisting of Het; O-Het; Het-Het; $-O-R^3$; $-NR^2R^3$; C_1-C_6 alkyl, which may be optionally substituted with one or more groups selected from the group consisting of R^4 and Het; C_2-C_6 alkenyl, which may be optionally substituted with one or more groups selected from the group consisting of R^4 and Het; C_3-C_6 saturated carbocycle, which may optionally be substituted with one or more groups selected from the group consisting of R^4 and Het; and C_5-C_6 unsaturated carbocycle, which may optionally be substituted with one or more groups selected from the group consisting of R^4 and Het; and

each R^4 is independently selected from the group consisting of $-OR^2$, $-C(O)-NHR^2$, $-S(O)_2-NHR^2$, halo, $-NR^2-C(O)-R^2$ and -CN.

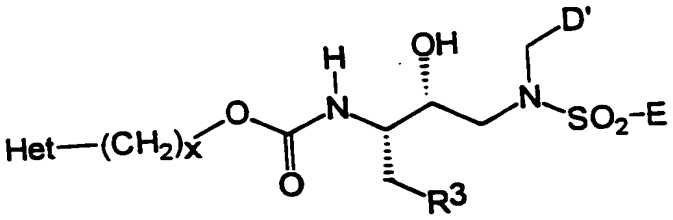
2. The compound according to claim 1, wherein said compound has the structure of formula XXII:



(XXII)

wherein A, D' and E are defined as in claim 1.

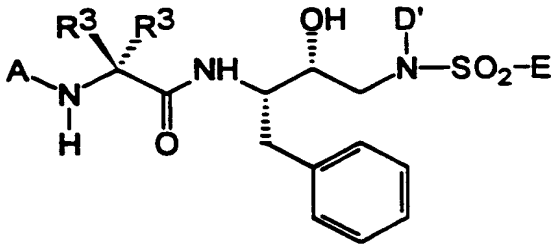
3. The compound according to claim 1, wherein said compound has the structure of formula XXIII:



(XXIII)

wherein x, Het, R^3, D' and E are defined as in claim 1.

4. The compound according to claim 1, wherein said compound has the structure of formula XXXI:



(XXXI)

wherein A, R^3, D' and E are defined as in claim 1.

5. A compound of formula I, wherein:

A is selected from the group consisting of H; $-R^1$-Het; $-R^1$-C_1-C_6 alkyl, which may be optionally substituted with one or more groups selected from the group consisting of hydroxy, C_1-C_4 alkoxy, Het and -O-Het; and $-R^1$-C_2-C_6 alkenyl, which may be optionally substituted with one or more groups selected from hydroxy, C_1-C_4 alkoxy, Het and -O-Het;

each R^1 is independently selected from the group consisting of -C(O)-, $-S(O)_2-$, -C(O)-C(O)-, -O-CO-, $-O-S(O)_2-$ and $-NR^2-S(O)_2-$;

each Het is independently selected from the group consisting of C_3-C_7 cycloalkyl; C_5-C_7 cycloalkenyl; C_6-C_{10} aryl; and 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, O and S, which may optionally be benzofused; wherein any member of said Het may be optionally substituted with one or more substituents selected from the group consisting of oxo, $-OR^2$, $-R^2$, $-N(R^2)_2$, $-R^2-OH$, -CN, $-CO_2R^2$, $-C(O)-N(R^2)_2$ and $-S(O)_2-N(R^2)_2$;

each R^2 is independently selected from the group consisting of H and C_1-C_3 alkyl;

B, when present, is $-NH-CH(R^3)-C(O)-$;

x is 0 or 1;

R^3 is selected from the group consisting of Het, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_6 cycloalkyl and C_5-C_6 cycloalkenyl, wherein any member of said R^3 may be optionally substituted with one or more substituents selected from the group consisting of $-OR^2$, $-C(O)-NH-R^2$, $-S(O)_n-N(R^2)_2$, Het and -CN;

n is 1 or 2;

D and D' are independently selected from the group consisting of Ar; C_1-C_4 alkyl, which may be optionally substituted with C_3-C_6 cycloalkyl or Ar; C_2-C_4 alkenyl, which may be optionally substituted with C_3-C_6 cycloalkyl or Ar; C_3-C_6 cycloalkyl, which may be optionally substituted or fused with Ar; and C_5-C_6 cycloalkenyl, which may be optionally substituted or fused with Ar; with the proviso that when D is attached to N, D may not be methyl or C_2 alkenyl;

Ar is selected from the group consisting of phenyl; 3-6 membered carbocyclic ring and 5-6 membered heterocyclic ring containing one or more heteroatoms selected from O, N and S, wherein said carbocyclic or heterocyclic ring may be saturated or unsaturated and optionally substituted with one or more groups selected from the group consisting of oxo, $-OR^2$, $-R^2$, $-N(R^2)_2$, $-N(R^2)-C(O)R^2$, $-R^2-OH$, $-CN$, $-CO_2R^2$, $-C(O)-N(R^2)_2$, halo and $-CF_3$;

E is selected from the group consisting of Het; $-O-R^3$; $-NR^2R^5$; C_1-C_6 alkyl, which may be optionally substituted with one or more R^4 or Het; C_2-C_6 alkenyl, which may be optionally substituted with one or more R^4 or Het; C_3-C_6 saturated carbocycle, which may optionally be substituted with one or more R^4 or Het; and C_5-C_6 unsaturated carbocycle, which may optionally be substituted with one or more R^4 or Het;

each R^4 is independently selected from the group consisting of $-OR^2$, $-C(O)-NHR^2$, $-S(O)_2-NHR^2$, halo and $-CN$; and

each R^5 is independently selected from the group consisting of H and R^3, with the proviso that at least one R^5 is not H.

6. The compound according to claim 2 or 3, wherein:

A is R^1-Het; and

D' is selected from the group consisting of C_1-C_3 alkyl and C_3 alkenyl, wherein said alkyl or alkenyl may optionally be substituted with one or more groups selected from the group consisting of C_3-C_6 cycloalkyl, $-OR^2$, -O-Ar and Ar.

7. The compound according to claim 3, wherein:

R^3 is selected from the group consisting of C_1-C_6 alkyl, C_2-C_6 alkenyl, C_5-C_6 cycloalkyl, C_5-C_6 cycloalkenyl and a 5-6 membered saturated or unsaturated heterocycle, wherein any member of said R^3 may optionally be substituted with one or more substituents selected from the group consisting of -OR^2, -C(O)-NH-R^2, -$S(O)_nN(R^2)(R^2)_2$, Het, -CN, -SR^2, -$C(O)_2R^2$, NR^2-C(O)-R^2; and

D' is selected from the group consisting of C_1-C_3 alkyl and C_3 alkenyl, wherein said alkyl or alkenyl may optionally be substituted with one or more groups selected from the group consisting of C_3-C_6 cycloalkyl, -OR^2, -O-Ar and Ar.

8. The compound according to claim 4, wherein:

A is R^1-Het;

each R^3 is independently C_1-C_6 alkyl, which may be optionally substituted with a substituent selected from the group consisting of -OR^2, -C(O)-NH-R^2, -$S(O)_nN(R^2)_2$, Het, -CN, -SR^2, -CO_2R^2, -NR^2-C(O)-R^2; and

D' is C_1-C_4 alkyl, which may be optionally substituted with a group selected from the group consisting of C_3-C_6 cycloalkyl, -OR^2, -O-Ar and Ar; and

E is selected from the group consisting of Het, Het-Het and -NR^2R^3.

9. A compound selected from the group consisting of:

(S)-N-1-(3-((3-Acetylamino-4-fluoro-benzenesulfonyl)-benzyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-

succinamide and (S)-N-1-(3-((4-Acetylamino-3-fluoro-benzenesulfonyl)-benzyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compounds 2);

(S)-N-1-(3-((5-Acetylamino-3-methyl-thiophene-2-sulfonyl)-benzyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 5);

(S)-N-1-(1-Benzyl-3-(benzyl-(5-isoxazol-3-yl-thiophene-2-sulfonyl)-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 6);

(S)-N-1-(3-((Benzo(1,2,5)oxadiazole-4-sulfonyl)-benzyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 9);

N-1-(1-(S)-Benzyl-3-(benzyl-(3-sulfamoyl-benzenesulfonyl)-amino)-2-(syn)-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 10);

(S)-N-1-(1-(S)-Benzyl-2-(syn)-hydroxyl-3-(isobutyl-(5-pyridin-2-yl-thiophene-2-sulfonyl)-amino)-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 12);

(S)-N-1-(3-((4-Benzenesulfonyl-thiophene-2-sulfonyl)-isobutyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 13);

(S)-N-1-(1-(S)-Benzyl-3-((4-fluoro-benzenesulfonyl)-isobutyl-amino)-2-(syn)-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 14);

(S)-N-1-(3-((4-Acetylamino-3-fluoro-benzenesulfonyl)-isobutyl-amino)-(1S,2 syn)-1-benzyl-

2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 15);

(S)-N-1-(3-((3-Acetylamino-4-fluoro-benzenesulfonyl)-isobutyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 16);

(S)-N-1-(1-(S)-Benzyl-3-((4-acetylamino-benzenesulfonyl)-isobutyl-amino)-2-(syn)-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 17);

(S)-N-1-(3-((5-Acetylamino-3-methyl-thiophene-2-sulfonyl)-isobutyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 18);

(S)-N-1-(3-((3-Acetylamino-benzenesulfonyl)-isobutyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 19);

(S)-N-1-(3-((Benzo(1,2,5)oxadiazole-4-sulfonyl)-isobutyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 20);

N-1-((1S-2 syn)-1-Benzyl-2-hydroxy-3-(1-isobutyl-3,3-dimethylsulfonylurea)-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 21);

N-1-(3-((4-Acetylamino-benzenesulfonyl)-isobutyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-(pyridin-2-yl-methoxycarbonyl)-succinamide (compound 22);

N-1-(3-((4-Acetylamino-benzenesulfonyl)-isobutyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-(pyridin-4-yl-methoxycarbonyl)-succinamide (compound 23);

N-1-(3-((4-Fluoro-benzenesulfonyl)-isobutyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-

(pyridin-2-yl-methoxycarbonyl)-succinamide (compound 26);

4-Fluoro-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide (compound 35);

3,4-Dichloro-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide (compound 37);

N-(4-(((2 syn,3S)-2-Hydroxy-4-phenyl-3-(pyridin-3-yl-methoxycarbonylamino)-butyl)-isobutyl-sulfamoyl)-phenyl)-acetamide (compound 44);

2,4-Dimethyl-thiazole-5-sulfonic acid-(1,1-dimethyl-ethoxycarbonylamino)-(2 syn,3S)-2-hydroxy-4-phenyl-butyl)-isobutyl-amide (compound 46);

N-(4-(((2 syn,3S)-2-Hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-sulfamoyl)-phenyl)-acetamide (compound 48);

4-Fluoro-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((R)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide and 4-Fluoro-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((R)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide (compounds 52);

Benzo(1,2,5)oxadiazole-5-sulfonic acid ((2 syn,3S)-2-hydroxy-4-phenyl-3-(pyridin-3-yl-methoxycarbonylamino)-butyl)-isobutylamide (compound 66);

N-(4-(((2 syn,3S)-2-Hydroxy-4-phenyl-3-((R)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-sulfamoyl-phenyl)-acetamide and N-(4-(((2 syn,3S)-2-Hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-sulfamoyl)-phenyl)-acetamide (compounds 86);

N-(2-Fluoro-5-(((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-sulfamoyl)-phenyl)-acetamide (compound 88);

N-(3-(((2 syn,3S)-2-Hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-sulfamoyl)-phenyl)-acetamide (compound 91);

4-Fluoro-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((R)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide (compound 93);

N-(4-(((syn)-2-Hydroxy-(S)-4-phenyl-3-((tetrahydro-furan-(R)-3-yl)-oxycarbonylamino)-butyl)-isobutyl-sulfamoyl)-phenyl)-acetamide (compound 94);

4-Fluoro-N-(2 syn,3S)-2-hydroxy-4-phenyl-3-((tetrahydro-furan-(R)-3-ylmethoxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide and 4-Fluoro-N-(2 syn,3S)-2-hydroxy-4-phenyl-3-((tetrahydro-furan-(S)-3-ylmethoxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide (compounds 97);

4-Fluoro-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-(pyridin-3-yl-methoxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide (compound 98);

4-Chloro-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-benzenesulfonamide (compound 99);

N-((2 syn,3S)-2-Hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-4-methoxy-benzenesulfonamide (compound 100);

4-Fluoro-N-(2-(syn)-hydroxy-3-((2-oxazolidon-(S)-4-yl)-methoxycarbonylamino)-4-(S)-phenyl-butyl)-N-isobutyl-benzenesulfonamide (compound 109);

Benzene-1,3-disulfonic acid 1-amide 3-((2 syn,3S)-2-hydroxy-4-phenyl-3-(3-(S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-amide (compound 112);

Furan-3-sulfonic acid (2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-amide (compound 113);

N-((3-Allyloxycarbonylamino)-(2 syn,3S)-2-hydroxy-4-phenyl-butyl)-N-cyclopentylmethyl-4-fluoro-benzenesulfonamide (compound 114);

N-Cyclopentylmethyl-N-((3-ethoxycarbonylamino)-(2 syn,3S)-2-hydroxy-4-phenyl-butyl)-4-fluoro-benzenesulfonamide (compound 115);

4-Chloro-N-cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 116);

4-Chloro-N-cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-(pyridin-3yl-methoxycarbonyl)-butyl)-benzenesulfonamide (compound 118);

N-(4-(Cyclopentylmethyl-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-sulfamoyl)-phenyl)-acetamide (compound 125);

3-Chloro-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide (compound 138);

4-Chloro-N-cyclopentylmethyl-N-(2-(syn)-hydroxy-3-((2-oxazolidon-4-(S)-yl-methyl)-oxycarbonylamino)-4-phenyl-butyl)-benzenesulfonamide (compound 139);

N-cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-4-methoxy-benzenesulfonamide (compound 140);

N-((3-allyloxycarbonylamino)-(2 syn,3S)-2-hydroxy-4-phenyl-butyl)-N-cyclopentylmethyl-4-methoxy-benzenesulfonamide (compound 141);

N-Cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-(3-pyridin-3-yl-methoxycarbonylamino)-butyl-4-methoxy-benzenesulfonamide (compound 142);

Pyridine-3-sulfonic acid ((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-amide, trifluoroacetic acid salt (compound 144);

5-Isoxazol-3-yl-thiophene-2-sulfonic acid ((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-amide (compound 145);

N-(4-((3-(Allyloxycarbonylamino)-(2 syn,3S)-2-hydroxy-4-phenyl-butyl)-cyclopentylmethylsulfamoyl)-phenyl)-acetamide (compound 146);

N-(4-(Cyclopentylmethyl-((2 syn,3S)-2-hydroxy-4-phenyl-3-(pyridin-3-yl-methoxycarbonylamino)-butyl)-sulfamoyl)-phenyl)-acetamide (compound 147);

N-Cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 148);

Pyridine-3-sulfonic acid cyclopentylmethyl-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-amide (compound 149);

Piperidine-1-sulfonic acid ((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-amide (compound 150);

N-4-((2-(syn)-Hydroxy-3-((2-methoxymethyl-allyloxycarbonylamino)-4-(S)-phenyl-butyl)-isobutyl-sulfamoyl)-phenyl)-acetamide (compound 155);

1-Acetyl-2,3-dihydro-1H-indole-6-sulfonic acid ((allyloxycarbonylamino)-(2 syn,3S)-2-hydroxy-4-phenyl-butyl)-cyclopentylmethyl-amide (compound 156);

1-Acetyl-2,3-dihydro-1H-indole-6-sulfonic acid cyclopentylmethyl-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-amide (compound 157);

N-Cyclohexylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-4-methoxy-benzenesulfonamide (compound 158);

N-Cyclohexylmethyl-4-fluoro-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 159);

N-(4-(Cyclohexylmethyl)-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-sulfamoyl-phenyl)-acetamide (compound 160);

N-((2 syn,3S)-2-Hydroxy-4-phenyl-3-(pyridin-4-yl-methoxycarbonylamino)-butyl)-N-isobutyl-4-methoxy-benzenesulfonamide (compound 163);

N-((2 syn,3S)-2-Hydroxy-4-phenyl-3-((syn)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-4-methyl-benzenesulfonamide (compound 165);

N-cyclopentylmethyl-4-hydroxy-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-(pyridin-3-yl-methoxycarbonylamino)-butyl)-benzenesulfonamide (compound 166);

N-((2 syn,3S)-2-Hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-4-nitro-benzenesulfonamide (compound 167);

4-Amino-N-((2 syn,3S)-2-Hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide (compound 168);

N-Cyclopentylmethyl-4-hydroxy-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 169);

N-Cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-4-nitro-benezensulfonamide (compound 170);

4-Amino-N-cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-

yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 171);

2,4-Diamino-N-cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 173);

4-Hydroxy-N-(2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide (compound 175);

N-Cyclopentylmethyl-4-fluoro-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 182);

3,4-Dichloro-N-cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 183);

Benzyloxycarbonyl-(L)-isoleucine-N-(5-((3-amino-(2 syn,3S)-2-hydroxy-4-phenyl-butyl)-isobutyl-sulfamoyl)-2-fluoro-phenyl)-acetamide (compound 187);

N-((4S,2S)-4-Cyclohexyl-2-hydroxy-3-((syn)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-cyclopentylmethyl-4-methoxy-benzenesulfonamide (compound 195);

and compounds 1001 through 1015.

10. The compound according to claim 9, said compound being selected from the group consisting of:

(S)-N-1-(1-(S)-Benzyl-2-(syn)-hydroxyl-3-(isobutyl-(5-pyridin-2-yl-thiophene-2-sulfonyl)-amino)-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 12);

(S)-N-1-(1-(S)-Benzyl-3-((4-fluoro-benzenesulfonyl)-isobutyl-amino)-2-(syn)-hydroxy-

propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 14);

(S)-N-1-(3-((4-Acetylamino-3-fluoro-benzenesulfonyl)-isobutyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 15);

(S)-N-1-(3-((Benzo(1,2,5)oxadiazole-4-sulfonyl)-isobutyl-amino)-(1S,2 syn)-1-benzyl-2-hydroxy-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 20);

N-1-((1S-2 syn)-1-Benzyl-2-hydroxy-3-(1-isobutyl-3,3-dimethylsulfonylurea)-propyl)-2-((quinoline-2-carbonyl)-amino)-succinamide (compound 21);

N-(4-(((2 syn,3S)-2-Hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-isobutyl-sulfamoyl)-phenyl)-acetamide (compound 48);

N-((2 syn,3S)-2-Hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-4-methoxy-benzenesulfonamide (compound 100);

4-Chloro-N-cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 116);

N-Cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-4-methoxy-benzenesulfonamide (compound 140);

N-Cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-(3-pyridin-3-yl-methoxycarbonylamino)-butyl-4-methoxy-benzenesulfonamide (compound 142);

N-Cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 148);

N-Cyclohexylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-4-methoxy-benzenesulfonamide (compound 158);

N-(4-(Cyclohexylmethyl)-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-sulfamoyl-phenyl)-acetamide (compound 160);

N-cyclopentylmethyl-4-hydroxy-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-(pyridin-3-yl-methoxycarbonylamino)-butyl)-benzenesulfonamide (compound 166);

4-Amino-N-((2 syn,3S)-2-Hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide (compound 168);

4-Amino-N-cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 171);

2,4-Diamino-N-cyclopentylmethyl-N-((2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-benzenesulfonamide (compound 173);

4-Hydroxy-N-(2 syn,3S)-2-hydroxy-4-phenyl-3-((S)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-isobutyl-benzenesulfonamide (compound 175); and

N-((4S,2S)-4-Cyclohexyl-2-hydroxy-3-((syn)-tetrahydrofuran-3-yloxycarbonylamino)-butyl)-N-cyclopentylmethyl-4-methoxy-benzenesulfonamide (compound 195).

11. The compound according to claim 1, wherein said compound has a molecular weight less than or equal to about 700 g/mol.

12. A compound according to claim 11, wherein said compound has a molecular weight less than or equal to about 600 g/mol.

13. A compound having the following structural and physicochemical characteristics:

(1) a first and a second hydrogen bond acceptor moiety, at least one of which is more highly polarizable than a carbonyl, said moieties being the same or different, and being capable of hydrogen bonding with the hydrogen atoms of the flap water molecule of an HIV aspartyl protease when the compound is bound thereto;

(2) substantially hydrophobic moieties which associate with the P_1 and P_1' binding pockets of said HIV aspartyl protease when the compound is bound thereto;

(3) a third hydrogen bonding moiety, which may be either a hydrogen bond donor or acceptor, capable of simultaneously hydrogen bonding to Asp25 and Asp25' of said HIV aspartyl protease when the compound is bound thereto;

(4) an additional occupied volume of space of at least 100 $Å^3$ when the compound is bound to the active site of said HIV aspartyl protease, said space overlapping with the volume of space that would be filled by a native substrate of said HIV aspartyl protease or a nonhyrolyzable isostere thereof;

(5) a deformation energy of binding of the compound to said HIV aspartyl protease of not greater than 10 kcal/mole; and

(6) a neutral or favorable enthalpic contribution from the sum of all electrostatic interactions between the compound and the protease when the compound is bound to said HIV aspartyl protease.

14. The compound according to claim 13, said compound having the structure of formula XL:

$$Z^1\text{-}Q^1\text{-}L^1\text{-}M\text{-}L^2\text{-}Q^2\text{-}Z^2 \qquad \text{(XL)}$$

wherein:

Q^1 and Q^2 are independently hydrogen bond acceptor moieties capable of binding with the hydrogen atoms of the flap water molecule of an HIV aspartyl protease, with the proviso that at least one of Q^1 or Q^2 is more highly polarizable than a carbonyl;

M is a hydrogen bonding moiety, which may be either a hydrogen bond donor or acceptor, capable of simultaneously hydrogen bonding to Asp25 and Asp25' of said HIV aspartyl protease;

L^1 and L^2 are independently acyclic or cyclic linker moieties; and

each of Z^1 and Z^2 may be optionally present and, if present, are independently selected from groups which occupy a volume of space overlapping with the volume of space that would be filled by the native substrate of said HIV aspartyl protease.

15. The compound according to claim 14, wherein at least one of Q^1 or Q^2 is a substituted sulfonamide.

16. A pharmaceutical composition effective against viral infection comprising a pharmaceutically effective amount of a compound according to any one of claims 1-4 and 13-14 and a pharmaceutically acceptable carrier, adjuvant or vehicle.

17. The pharmaceutical composition according to claim 16, further comprising an additional anti-viral agent.

18. A method for using of a compound according to any one of claims 1-4 and 13-14 as a

therapeutic agent against viral infection, said virus requiring an aspartyl protease for an obligatory life cycle event.

19. The method according to claim 18, wherein said virus is HIV-1, HIV-2, or HTLV.

20. The use according to any one of claims 1-4 and 13-14, for inhibiting enzymatic activity in an aspartyl protease.

21. The use according to claim 20, wherein said aspartyl protease is HIV protease.

22. A method for preventing HIV infection in a mammal comprising the step of administering to said mammal a pharmaceutically effective amount of a pharmaceutical composition according to claim 16 or 17.

23. A method for treating HIV infection in a mammal comprising the step of administering to said mammal a pharmaceutically effective amount of a pharmaceutical composition according to claim 16 or 17.

24. The method according to claim 22 or 23, wherein said step of administering comprises oral administration or administration by injection.

25. A method for identification, design, or prediction of an HIV protease inhibitor comprising the steps of:

(a) selecting a candidate compound of defined chemical structure containing a first and a second hydrogen bond acceptor moiety, at least one of which is more highly polarizable than a carbonyl, said

moieties being the same or different; a third hydrogen bonding moiety, which may be either a hydrogen bond donor or acceptor; and at least two substantially hydrophobic moieties;

(b) determining a low-energy conformation for binding of said compound to the active site of an HIV aspartyl protease;

(c) evaluating the capability of said first and second hydrogen bond acceptor moieties to form hydrogen bonds to the flap water molecule of said HIV aspartyl protease when said compound is bound thereto in said conformation;

(d) evaluating the capability of said substantially hydrophobic moieties to associate with the P_1 and P_1' binding pockets of said HIV aspartyl protease when said compound is bound thereto in said conformation;

(e) evaluating the capability of said third hydrogen bonding moiety to form hydrogen bonds to Asp25 and Asp25' of said HIV aspartyl protease when said compound is bound thereto in said conformation;

(f) evaluating the overlap of the occupied volume of said compound when said compound is bound to said HIV aspartyl protease in said conformation and the occupied volume of a native substrate of HIV aspartyl protease or a nonhydrolyzable isostere thereof, when said polypeptide is bound to said HIV aspartyl protease;

(g) evaluating the deformation energy of binding of said compound to said HIV aspartyl protease;

(h) evaluating the enthalpic contribution of the sum of all electrostatic interactions between said compound and said HIV

aspartyl protease when said compound is bound thereto in said conformation; and

(i) accepting or rejecting said candidate compound as an HIV protease inhbitor based upon the determinations and evaluations carried out in steps (b) through (h).

26. An HIV protease inhibitor identified, designed or predicted by the method according to claim 25.

27. The HIV protease inhibitor according to claim 26, wherein said inhibitor has the structure of formula XL:

$$Z^1\text{-}Q^1\text{-}L^1\text{-}M\text{-}L^2\text{-}Q^2\text{-}Z^2 \qquad \text{(XL)}$$

wherein:

Q^1 and Q^2 are independently hydrogen bond acceptor moieties capable of binding with the hydrogen atoms of the flap water molecule of an HIV aspartyl protease, with the proviso that at least one of Q^1 or Q^2 is more highly polarizable than a carbonyl;

M is a hydrogen bonding moiety, which may be either a hydrogen bond donor or acceptor, capable of simultaneously hydrogen bonding to Asp25 and Asp25' of said HIV aspartyl protease;

L^1 and L^2 are independently acyclic or cyclic linker moieties; and

each of Z^1 and Z^2 may be optionally present and, if present, are independently selected from groups which occupy a volume of space overlapping with the volume of space that would be filled by the native substrate of said HIV aspartyl protease.